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EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/003,759	WICHER ET AL.
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652

-- The MAILING DATE of this communication appears in the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 August 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) 23-29 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-22 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 23 October 2001 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1, 5.

4) Interview Summary (PTO-413) Paper No(s). _____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____.

DETAILED ACTION

Claims 1-29 are still at issue and are present for examination. Claims 1-22 are now under consideration. Claims 23-29 remains withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-22 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that coexamination of all of Groups I-II would not be an undue burden on the Examiner. Applicants also maintain that a similar set of claims presented in the parent application 09/594,884 were not restricted by the Examiner and were examined as a single group. While Examiner acknowledges the above, applicants are reminded that restriction is at the discretion of the Examiner. During the examination of the parent application Examiner realized that the additional claims of group II drawn to a method of making the variant enzyme (and which have been restricted in the present application) were found to be burdensome for search and examination. Hence claims 23-29 were restricted in this application. Furthermore, claims 23-29 clearly present themselves as an independent invention as explained in the previous Office action. Therefore, applicant's arguments to rejoin claims of group I with claims of group II is not found persuasive because while the searches for the two groups overlap, they are not coextensive. The search for Group II requires the search of subclasses unnecessary for the search of elected Group I. For example, search of Group I would require search of subclass 435/69.1 and search of Group II would require search of subclass 435/471.

The requirement is still deemed proper and is therefore made FINAL.

Claims 23-29 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claims 1 and 15 are objected to because of the following informalities: Claims 1 and 15 recite the word "hydrolase" with incorrect spelling. Appropriate correction is required.

Claims 1 and 15 are objected to because of the following informalities: Claims 1 and 15 recite the word "length" with incorrect spelling. Appropriate correction is required.

Claims 1, 4, 7, 10, 11, 14, 15, and 16, are objected to because of the following informalities: Claims 1, 4, 7, 10, 11, 14, 15, 16 recite the phrase "isolated nucleic acid". Even though, it is commonly accepted in the art that a nucleic acid means a sequence of nucleotides, for reasons of legal clarity, examiner request applicants to amend the claim to recite "an isolated nucleic acid molecule" or "an isolated nucleic acid sequence" or "an isolated polynucleotide". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 5-6, 8-9, 12-13, 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-3, 5-6, 8-9, 12-13, 17-22 all recite the phrase either "A construct" or "the construct". It is not clear to the Examiner as to what applicants mean by a construct. It appears that applicants intend to claim "a nucleic acid construct". If this were so, amending the claim accordingly would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 15-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence with SEQ ID NO:3 or DNA having the recited structural limitations as claimed in claims 4, 7, 10 or 11 which encode a protein having thermostable cellulase activity, does not reasonably provide enablement for any variant DNA sequence (in which nucleotides are substituted, inserted or deleted) from any source encoding a variant glycosyl hydrolase of family 12 and wherein said nucleic acid sequence is truncated such that one or more amino acid residues corresponding to position one to about 40 are deleted in the polypeptide encoded by said nucleic acid sequence. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-3, 15-20 are so broad as to encompass any DNA, which encodes a variant family 12 glycosylhydrolase, and vectors and host cells comprising such DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for a variety of processes including recombinant protein preparation. Applicants may also use the DNA sequences in the form of oligonucleotide probes to screen a cDNA library and for identification of mRNA and in designing PCR reactions. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent homology can be used for recombinant protein preparation or as a probe for either identifying mRNA or for screening a cDNA library, changing the nucleotide sequences as proposed by the applicants and/or addition/deletion of substantial amount of nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:3 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of

nucleotide sequences that will hybridize to several unrelated mRNAs instead of hybridizing specifically to the mRNA of interest and similarly may hybridize to cDNAs totally unrelated to the protein of interest while screening a cDNA library. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single thermostable cellulase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence that can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding a protein having thermostable cellulase activity because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of thermostable cellulase DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any thermostable cellulase nucleotide with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope

of the claims broadly including any DNA encoding thermostable cellulase of family 12. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-3, 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of variant DNA molecules encoding variant thermostable cellulase of family 12.

The specification does not contain any disclosure of the structure and function of all variant DNA sequences that a variant thermostable cellulase. The genus of DNAs that comprise these above DNA molecules is a large variable genus with different structures and the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as obvious over Halldorsdottir et al. (Appl. Microbiol. Biotechnol., 1998, Vol. 49:277-284, and the enclosed sequence alignment), Gilkes et al. (Microbiol. Rev., 1991, Vol. 55(2):303) and the high level of knowledge existing in the art. This rejection is based upon the public availability of printed publications. Claims 1-22 of the instant application are drawn to a variant polynucleotide sequence encoding a variant thermostable cellulase with a SEQ ID NO:2 wherein one or more residues from position one to position 40 are deleted, or wherein 52-82 nucleotides from the 5' end are deleted (as depicted in claim 7), or wherein 88-112 nucleotides from the 5' end are deleted (as depicted in claim 11), or polynucleotides comprising sequences for a fusion protein comprising the sequences of the thermostable cellulase vectors and host cells comprising the same (claims 19-20, 22-23, 26, 27, 30-31) and methods of producing the thermostable cellulase. Halldorsdottir et al. teach the cloning, sequencing and over expression of a *R..marinus* gene encoding a thermostable cellulase of glycosyl hydrolase family 12. They also provide the polynucleotide sequence as a GenBank deposit (GenBank Accession No.RMU72637, 11 May 1999). The reference also teaches vectors and host cells and method of making the thermostable cellulase from culturing the host cells. However, the reference does not teach the variant thermostable cellulases which are expressed by

polynucleotides in which 40, 82, 112 nucleotides are deleted from the 5' end of fusion proteins comprising the thermostable cellulase of family 12.

Gilkes et al. teach the structural elements in cellulases and xylanases. The reference teaches that cellulases can be classified into several families based on the structural similarities and that the structure of the thermostable cellulases comprises linkers, repeated sequences, cellulose-binding domains and catalytic domains. The reference compares most thermostable cellulases in terms of the domains and specifically the amino acids which comprise these domains. The reference also teaches which domains among these are essential and what roles these domains specifically play during the catalytic action of the enzyme.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Halldorsdottir et al. with that of Gilkes et al. and construct vectors in which nucleotides from the 5' end were successively deleted. It would also have been obvious to one of ordinary skill in the art to combine the teachings of Halldorsdottir et al. with that of the high level of knowledge existing in the art of molecular biology to construct fusion proteins. One of ordinary skill in the art would have been motivated to construct the deletions in order to determine the different roles or requirements of amino acid domains for cellulase activity in the newly discovered enzyme based on the teachings of Gilkes et al. and one skilled in the art would have been motivated to construct fusion proteins using domains such as cellulose binding domain (for either strong binding or weak binding depending on the application) and the thermostable cellulase taught by Halldorsdottir et al. One of ordinary skill in the art would have a reasonable expectation of success since Halldorsdottir et al. teach the cloning, sequencing and over

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expression of a thermostable cellulase from *R.marinus* and Gilkes et al. teach the roles and importance of domains in such thermostable cellulases.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

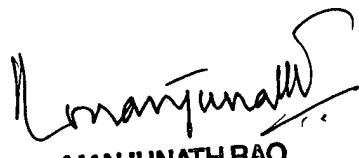
None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

Manjunath N. Rao
October 20, 2002



MANJUNATH RAO
PATENT EXAMINER